

DELIVERY OF THERAPEUTIC BIOLOGICALS FROM IMPLANTABLE TISSUE MATRICES

Abstract

5 Normal cells, such as fibroblasts or other tissue or organ cell types, are genetically engineered to express biologically active, therapeutic agents, such as proteins that are normally produced in small amounts, for example, MIS, or other members of the TGF-beta family HerceptinTM, interferons, and anti-angiogenic factors. These cells are seeded into a matrix for implantation into the

10 patient to be treated. Cells may also be engineered to include a lethal gene, so that implanted cells can be destroyed once treatment is completed. Cells can be implanted in a variety of different matrices. In a preferred embodiment, these matrices are implantable and biodegradable over a period of time equal to or less than the expected period of treatment, when cells engraft to form a functional

15 tissue producing the desired biologically active agent. Implantation may be ectopic or in some cases orthotopic. Representative cell types include tissue specific cells, progenitor cells, and stem cells. Matrices can be formed of synthetic or natural materials, by chemical coupling at the time of implantation, using standard techniques for formation of fibrous matrices from polymeric

20 fibers, and using micromachining or microfabrication techniques. These devices and strategies are used as delivery systems *via* standard or minimally invasive implantation techniques for any number of parenterally deliverable recombinant proteins, particularly those that are difficult to produce in large amounts and/or active forms using conventional methods of purification, for the

25 treatment of a variety of conditions that produce abnormal growth, including treatment of malignant and benign neoplasias, vascular malformations (hemangiomas), inflammatory conditions, keloid formation, abdominal or plural adhesions, endometriosis, congenital or endocrine abnormalities, and other conditions that can produce abnormal growth such as infection. Efficacy of

30 treatment with the therapeutic biologicals is detected by determining specific criteria, for example, cessation of cell proliferation, regression of abnormal tissue, or cell death, or expression of genes or proteins reflecting the above.